REMARKS

Claims 4-14 are pending in the application. Claims 4, 5, 10, and 11 stand rejected under 35 U.S.C. 102(b) over Eritja and claims 7-9 stand rejected under 35 U.S.C. 103(a). Rejections of claims 5 and 10 under 35 U.S.C. 102(b) over Switzer and Piccirilli, claims 4, 6, 8-9, and 11-14 under 35 U.S.C. 102(a), and claims 4-14 under the judicially created doctrine of obviousness-type double patenting, which were asserted in the Office Action mailed July 5, 2001, have been withdrawn.

Applicants have amended claim 4 to clarify that the method requires that when the non-standard nucleotide in the template is a purine a derivatized pyrimidine is incorporated into the oligonucleotide opposite the non-standard nucleotide at the preselected site, and when the non-standard nucleotide in the template is a pyrimidine, a derivatized purine is incorporated into the oligonucleotide opposite the non-standard nucleotide at the preselected site. Newly added claims 15-18 are comparable to claims 6 and 12-14, which the Examiner indicated would be allowable if written in independent form.

In view of the amendments above and the arguments below, Applicants respectfully request reconsideration on the merits of the application.

Rejections under 35 U.S.C. 102(b)

A. Rejection of claims 4, 5, 10, and 11 as being anticipated by Eritja

Claims 4, 5, 10, and 11 stand rejected under 35 U.S.C. 102(b) as being anticipated by Eritja (NAR 14:8135-8153, 1986). Eritja is cited as teaching a method of making an oligonucleotide using a template containing a non-standard nucleotide (xanthine) by contacting the template with a mixture of nucleotide triphosphates and forming an oligonucleotide complementary to a portion of the template containing the xanthine by enzymatic polymerization, and incorporation of 9-(β-D-2'-deoxyribofuranosyl)-2-aminopurine triphosphate (dAPTP) opposite xanthine.

Claim 4, from which claims 5, 10, and 11 depend, has been amended to clarify that in contrast to Eritja, which teaches misincorporation of 2-aminopurine opposite xanthine, also a purine, the method of the present invention requires incorporation into an oligonucleotide of a derivatized pyrimidine opposite a non-standard purine or a derivatized purine opposite a non-standard pyrimidine.

Applicant respectfully submits that none of claims 4, 5, 10, or 11 is anticipated by the Eritja publication, because Eritja does not teach all of the limitations of claim 4, as amended. The non-standard purine base xanthine has incorporated opposite it the noncomplementary

base 2-aminopurine, as opposed to incorporating a derivatized purine opposite a non-standard pyrimidine, or a derivatized pyrimidine opposite a non-standard purine, as required by claims 4, 5, 10, and 11.

In view of the foregoing, Applicant respectfully requests that the rejection of the claims under 102(b) as being anticipated by Eritja be withdrawn.

Rejections under 35 U.S.C. 103(a)

Claims 7-9, which depend from claim 4, stand rejected under 35 U.S.C. 103(a) as being unpatentable over Eritja *et al.* The Examiner asserts that incorporation of labeled nucleotides into oligonucleotides by primer extension is well known.

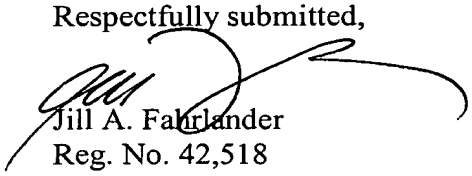
Applicant respectfully submits that the Examiner has failed to establish a prima facie case of obviousness, which requires (1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) a reasonable expectation of success; and (3) the art reference or combination of references must teach all of the claim limitations (MPEP 2142).

As Applicant pointed out above in the discussion of the rejection of claims 4, 5, 10, and 11 under 102(b), Eritja does not teach or suggest all of the limitations of claim 4. Specifically, Eritja does not teach or suggest incorporating a derivatized purine opposite a non-standard pyrimidine, or a derivatized pyrimidine opposite a non-standard purine, as required by claim 4. Therefore, Eritja does not teach or suggest all of the claim limitations of claims 7-9, which depend from and further limit claim 4.

As the application is now in condition for allowance, Applicants request allowance of the claims. Should the Examiner feel that any other point requires consideration or that the form of the claims can be improved, the Examiner is invited to contact the undersigned at the number listed below.

This response is accomanied by a Notice of Appeal, a request for a three month extension of time, and the appropriate fees. No other fee is believed due in connection with this submission. Please charge any fee due or credit any overpayment of fees to Deposit Account No. 50-0842.

Respectfully submitted,



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MARKED UP VERSION OF CLAIMS SHOWING CLEARLY THE AMENDMENTS

4. (Amended) A method of making an oligonucleotide, the method comprising:

providing a template oligonucleotide comprising a sequence of nucleotides, the template comprising at least one non-standard nucleotide selected from the group consisting of purines and pyrimidines at a preselected site in the sequence;

contacting the template with a mixture of nucleotide triphosphates, the mixture comprising nucleotide triphosphates that are complementary to the nucleotides of the template, wherein the nucleotide triphosphate complementary to the non-standard nucleotide at the preselected site comprises a derivatized nucleotide; and

forming an oligonucleotide complementary to a portion of the template comprising the non-standard nucleotide by enzymatic polymerization of the nucleotide triphosphates in a sequence complementary to the portion of the template, wherein a derivatized purine complementary to the non-standard nucleotide is incorporated opposite the non-standard nucleotide at the preselected site if the non-standard nucleotide is a pyrimidine, or wherein a derivatized pyrimidine complementary to the non-standard nucleotide is incorporated opposite the non-standard nucleotide at the preselected site if the non-standard nucleotide is a purine.